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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,025	04/24/2001	Judith Aronhime	1662/52602	6176

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/841,025	ARONHIME ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *161,162,166,261,262,264,265 and 269* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *161,162,166,261,262,264,265 and 269* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicants dated Jan. 3, 2006 have been entered and considered carefully.

Claims 1-160, 163-165, 167-260, 263, 266-268, 270-279 have been canceled.

Claims 161-162, 166, 261-262, 264-265, 269 are pending.

2. The rejection of claims 264-265, 269 under 35 USC 112 second paragraph is maintained for reason of record and in view of the current amendment is also applicable to claims 161-162, 166, 261-262.

It is very confusing as to what is the scope of the claims. Please note that one category of patentable invention is a "product". A novel or unobvious chemical product is identified first by its "chemical nature, i.e. elemental content and their ratios. It is a well known in the pharmaceutical art that drugs are known to have polymorphic forms (see US pharmacopia #23, national formulary #18,1995 of record). It was well known "fact" that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice. Thus *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 2). Therefore, for a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavalability, easy of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p.185).

In the field of crystal chemistry (Evans, p.284-285), it is well recognized that hydrates which containing coordinating water for which when the water is removed will loss its crystalline structure are "isolated site hydrates" which can be identifiable by a different molecular formula. Other hydrates known as clathrates or channel hydrates etc. (see Brittain p.145-157) which are identical crystalline products with water/solvents being trapped in the interstices among the crystalline frame works and such inclusion is strictly purely by mechanical

constraints. The product is the same crystalline molecules with *impurities* mechanically trapped in its interstices (Evans p.396).

The instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug. There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction pattern, melting point etc. Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268. Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable.

In addition, it is noted that the term "Zolpidem hemitartrate Form D" are defined on page 3 to be i) zolpidem hemitartrate Form D monohydrate;

ii) zolpidem hemitartrate Form D characterized by a water content of about 2.3% to about 2.7% by weight;

iii) zolpidem hemitartrate Form D hemiethanolate;

iv) zolpidem hemitartrate Form D characterized by an X-ray diffraction pattern having peaks at about 7.1, 9.5, 14.2, 19.6 and 24.5$\pm$ 0.2 degrees two theta.

It is unclear "what" is the claimed product. Are all Form D hemitartrate having the same X-ray? Are they the same product or different product ?

The rejection is proper and maintained for reason of record.

3. The rejection of claim 166 under 35 USC 102(b) over Benincasa US 5,891,891 is maintained for reason of record.

Please note that at physiological environment, all compounds are in a liquid phase (see Rowland Clinical pharm. P.123). It is unclear what does PXRD offer any limitation as to how the "treatment" of a drug is being accomplished. Especially, the prior art method is treating insomnia using a therapeutically effective amount of Zolpidem hemitartrate CAS Registry no. 99294-93-6 for which the instantly described Zolpidem hemitartrate recited supra as (i)-(iv) are

all having identical chemical nature. No evidence was offered that the instant claims zolpidem hemitartrate *does not depend* on the chemical nature of the product but the physical property for such efficacy. Please note that *in the strictest sense, polymorphs are different crystalline forms of the **same pure substance** in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 2).

4. The rejection of claims 161, 166, 262, 264, 265, 269 over 35 USC 103(a) over Ettema I '360 in view of Ettema II '460 further in view of Brittain is maintained for reason of record.

In the first place, it is unclear what is the relevancy of applicants' argument. Again, the argument that prior art was without PXRD does not offer any rebuttal to the factual issue of the application. Physical property of a product is innate to that product whether the reference names such or not. Just like when one disclosed benzene and benzene b.p. 80°C are identical because if it is C_6H_6 or benzene it has a boiling point of 80°C.

Applicants offered no explanation as to the Zolpidem hemitartrate recited supra as (i)-(iv) as disclosed in the specification to be "one product" or at least four products. Further, it is well recognized in the pharmaceutical art that multiple forms may occur in drugs which will give different X-ray pattern but not all of them are polymorphs (see US pharmacopia). In addition, X-ray diffraction pattern are identification of "crystals" i.e. physical forms, it does not provide information on the chemical nature. As it is well recognized in the art, inclusion crystals or clathrates are "identical" crystalline form with mechanically trapped impurities. Such trapped impurity, although may change the X-ray diffraction pattern (US pharmacopia or Yang et al. showing scientific basis of the explanation) are not different crystals. The prior art disclosed a product prepared from methanol, even though the PXRD of the product was not disclosed but innate to this product. Evidenced by the innate nature of Zolpidem salt to be clathrates, the instant provision of PXRD is a mere variation of the same crystal of the prior art. There is no evidence in the record that the instantly claimed product, even with the PXRD is actually a "different" crystalline form not a modified PXRD due to the solvent effect.

Further, even if (i)-(iv) are different forms, it is *the **same pure substance** in which the molecules have different arrangements,* without a patentability basis of an advantage in terms of stability, formulation, solubility, bioavalability, easy of purification, preparation or synthesis,

hydroscopicity, recovery or prevention of precipitation etc. (see Brittain p.2, 185) it is prima facie obvious over the known product.

5. Newly cited references are provided for applicants' convenience of the state of the art which do not change any issue or basis of rejection of record.

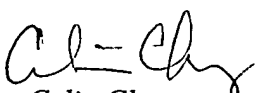
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



OACS/Chang
Mar. 15, 2006

Celia Chang
Primary Examiner
Art Unit 1625